

#### REMARKS

Applicants thank the Examiner for the courtesy extended to their representative, Jane Gunnison, in granting a telephone interview on July 23, 2003.

Applicants have amended the specification to more clearly set forth the priority claim. Applicants have canceled claims 17, 18, 20, 21 and 23, without prejudice, and expressly reserve the right to prosecute the subject matter of the canceled claims in one or more patent applications that claim priority under 35 U.S.C. § 120 from this application. Upon entry of the amendments, claims 24-27 will be pending in the application.

Applicants have added claims 24-27 to more clearly set forth the subject matter that they wish to pursue in this application. Claim 24 is directed to a method for inhibiting a pathological increase in collagen volume in heart tissue by administering a compound of the recited formula. Claim 25, which depends from claim 24, specifies that the compound to be administered is halofuginone. Support for these claims may be found in the application, as filed, for example, at page 26, line 21 to page 27, line 2, and in Figure 6.

Claim 26 is directed to a method for inhibiting the expression of collagen  $\alpha 1(I)$  mRNA expression in heart tissue by administering a compound of the recited formula. Claim 27, which depends from claim 26, specifies that the compound is halofuginone. Support for these claims may be found in the application, as filed, for example, at page 27, lines 3-14 and in Figure 7.

None of these amendments adds new matter. Applicants believe that the amendments put the application in condition for allowance. Accordingly, applicants request

entry of the amendments and reconsideration of the claims.

Acknowledgment of Domestic Priority

Applicants note that on the page entitled Office Action Summary of the June 24, 2003 Office Action, Item 14 is not checked off. Item 14 is acknowledgment of domestic priority under 35 U.S.C. § 119(e) to a provisional application. This application claims priority from, *inter alia*, a United States provisional application. Accordingly, applicants request acknowledgment of such domestic priority.

Irregularities in Office Action

Applicants note that page 2 of the June 24, 2003 Office Action incorrectly states:

III. The rejection of claims 17-18, 20-21 and 23 under 35 U.S.C. 103(a) will be maintained for the reason of record.

Applicants further note that on page 4 of the June 24, 2003 Office Action, the Examiner states:

Claims 15 and 17-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergeron et al. (The American Society of Hematology, 1998) in view of Martell (US 3758540) and Gasparini et al. (WO 95/1663 [sic]).

During a July 23, 2003 telephone interview, the Examiner agreed that both of the above-described passages were in error. The Examiner stated that No. III on p. 2 of the Office Action should have indicated that the rejection of those claims under § 102(b) was maintained. The rejection under 103 set forth on pages 3-4 of the Action should be deleted. Accordingly, applicants have not addressed that rejection.

Finally, the Examiner stated that in view of the

errors, the finality of the January 24, 2003 Office Action was withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 21 and 23 stand rejected under 35 U.S.C. § 112, second paragraph, as "indefinite" in the use of the term "substantially prevent". Applicants' cancellation of those claims, without prejudice obviates the rejection. However, applicants do not acquiesce in the rejection. The application, as filed, demonstrates that a compound of the recited formula, in particular halofuginone, partially prevents an the increase in the amount of collagen in a cardiac fibrosis model.

Specifically, Fig. 6 shows that in the model (i.e., animals receiving angiotensin II (Ang II)), the heart tissue showed a large increase in collagen volume compared to control animals and that halofuginone prevented most but not all of that increase. Referring to Fig. 6, the application, as filed, describes this effect as "substantially inhibited" fibrosis and states that halofuginone showed a strong ability to prevent the increase in collagen volume (page 26, lines 24-28 and line 33 to page 25, line 2).

Further, Fig. 7 shows that halofuginone partially prevents collagen mRNA expression in heart tissue. Referring to Fig. 7, the application, as filed, states that halofuginone substantially reduced but did not completely inhibit such expression (page 27, lines 9-11).

In view of this disclosure, one of ordinary skill in the art would understand what is meant by "substantially preventing" cardiac fibrosis.

Rejection Under 35 U.S.C. 102(b)

Claims 17, 18, 20, 21 and 23 (all of the previously pending claims) stand rejected under 35 U.S.C. § 102(b) as anticipated by United States patent 5,449,678 ("Pines"). Applicants' cancellation of those claims, without prejudice, obviates that rejection.

It is not clear to applicants what the Examiner meant in characterizing certain arguments in the October 7, 2002 Response as "spurious" (June 24, 2003 Office Action, p. 6). However, applicants wish to make clear on the record that the arguments represent a good faith attempt to respond to the rejections.

Claims 24 and 25 are directed to methods for inhibiting a pathological increase in collagen volume in heart tissue. The claims are based on experiments described in the instant application but not described in Pines.

Similarly, claims 26 and 27 are directed to methods for inhibiting the expression of collagen  $\alpha 1(I)$  mRNA in heart tissue. Pines contains no disclosure of the effect of the recited compounds on collagen mRNA expression.

Accordingly, claims 24-27 are novel over Pines.

Rejection for Non-statutory Double Patenting

Claims 17, 18, 20, 21 and 23 stand rejected under the judicially created doctrine of double patenting over claim 1 of Pines. Applicants' cancellation of those claims obviate this rejection.

Applicants believe that the application is now in

condition for allowance. In view of the foregoing, thus, applicants request reconsideration of the application and allowance of claims 24-27.

Respectfully submitted,

Jane Gunnison (enf)  
Jane T. Gunnison (Reg. No. 38,479)  
Attorney for Applicants  
c/o FISH & NEAVE  
1251 Avenue of the Americas  
New York, New York 10020-1104  
Tel.: (212) 596-9000